

# Fetal Growth and Body Proportion during Pre-Eclamptic Pregnancy

### Abstract

**Purpose:** To evaluate the effects of mild and severe PE on fetal growth and body proportion, measurement at serial ultrasound (US) examinations. Five to 7% of all pregnancies are complicated by preeclampsia (PE). Some forms of intrauterine growth restriction (IUGR) have been etiologically linked to PE, based on similar placental disease- abnormal implantation.

**Materials and Methods:** Women (n=400) who had singleton pregnancies and underwent two or more second- and third-trimester obstetric US examinations were included in our study. The women were divided in three groups: 300 normotensive pregnancies (controls), 67 pregnancies with mild PE (MP) and 33 pregnancies with severe PE (SP). Inadequate fetal growth was defined as growth at or below 10<sup>th</sup> percentile. We calculated US measurements between fetuses from normotensive and PE pregnancies (MP and SP).

**Results:** In newborns of women with PE, mean birth weight and length were lower than in births without PE. Fetuses in PE pregnancies from 26 week of gestation (wg) with US scan had lower biometric parameters vs. then of normotensive pregnancies, especially values of abdominal circumference and femur length. In PE pregnancies, there could be faster aging of placenta and oligohydramnion. This is time before clinical onset of PE.

**Conclusion:** Our results support the hypothesis that PE is a heterogeneous disorder which involving placental dysfunction and IUGR, often with asymmetric fetal body proportion and reduced fetal length. The results suggest that US measurements of fetal size are important predictors for PE and birth outcomes.

Keywords: Fetal growth; Intrauterine growth restriction; Pre-eclampsia; Ultrasound

**Abbreviations:** AC: Abdominal Circumference; AFI: Amniotic Fluid Index; BMI: Body Mass Index; BPD: Biparietal Diameter; FL: Femur Length; GA: Gestational Age; HC: Head Circumference; IUGR: Intrauterine Growth Restriction; LMP: Last Menstrual Period; PE: Pre-Eclampsia; UPC: Utero Placental Circulation; US: Ultrasound; wg: Week of Gestation

## Introduction

Preeclampsia is a multi-system disorder of unknown etiology. Women with preeclampsia usually develop raised blood pressure and proteinuria. Preeclampsia is also associated with abnormalities of coagulation system, disturbed liver function, renal failure and cerebral ischemia [1]. PE is characterized by vasospasm, increased peripheral vascular resistance, and thus reduced organ perfusion [1,2].

Also, it's well known that PE is associated with reduced fetal size. Fetal growth is dependent on genetic, placental and maternal factors. Intrauterine growth restriction (IUGR) refers to a condition in which a fetus is unable to achieve its genetically determined potential size. The most widely used definition of IUGR is a fetus whose estimated weight is below 10<sup>th</sup> percentile for its gestational age [3-5].

IUGR occurs when gas exchange and nutrient delivery to the fetus are not sufficient to allow it to thrive in utero. This process can occur primarily because of maternal disease causing decreased oxygen-carrying capacity, a dysfunctional oxygen delivery system **Research Article** 

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secondary to maternal vascular disease, or placental damage resulting from maternal disease [4-8].

Ultrasound (US) fetal biometry is the most widespread method used to establish gestational age, estimate fetal size and monitor its growth. US fetal biometry is gold standard for assessing fetal growth. The most commonly used measurements are the biparietal diameter, head circumference, abdominal circumference and femur length [9]. Accurate dating of the pregnancy is essential in the use of any parameter. In the absence of reliable dating, serial scans at two or three weeks intervals must be performed to identify IUGR [5,8,10].

The basic idea of our study is: early identification of eventually IUGR and fetus development, placental maturation and amount of amniotic fluid using US method. The objective of the present study was to evaluate the effect of mild and severe PE on fetal growth and body proportion. We hypothesized that inadequate fetal growth at US examinations would indicate development of PE, with combination of other risk factors.

# **Materials and Methods**

The research was conducted in the Clinical Hospital "Dr Trifun Panovski" in Bitola, Macedonia, Department of gynaecology and obstetrics. These patients had been admitted during the period of May 1<sup>st</sup> 2008 to August 1<sup>st</sup> 2009. This study protocol was approved by the Director of Clinical Hospital in Bitola, Macedonia and the Ethics committee of School of Medicine University of Belgrade, Serbia. A written consent was provided by all participants. The study included 400 participants. Concerning recommendations of Ethics committee, this prospective study should be content 300 normotensive pregnant as control and 100 preeclamptic pregnant. The preeclamptic women later on, based on clinic and laboratory parameters, were divided in two subgroups: women with mild and severe preeclampsia. This study wasn't limited by the time and when we reach the demanded numbers of patients, we stop the further research. The study included 400 participants, between 15-43 years (average age  $27.65 \pm 5.04$ ), divided in three groups: control group (Controls, n=300 normotensive pregnancies); group with mild preeclampsia (Mild PE, n=67) and group with severe preeclampsia (Severe PE, n=33).

The participants were healthy women with no history of any chronic disease, with singleton pregnancy, without chromosomal or congenital abnormalities, with exact date of the last menstrual period and regular menstrual period.

Women with multiple fetuses, without valid data on the last menstrual period and valid ultrasound measurement and chronic maternal disease were excluded. The criteria to determine the exact pregnancy stage is based on the following reliable criteria: anamnestical, obstetrical and ultrasound scan, which means that the information of the last period is corresponding with the results from the obstetrical examination and the ultrasound scan. The first examination was performed in the period 6-12 wg. All patients started the pregnancy with normal blood pressure, i.e. on their first visit they didn't have artery pressure above 120/80 mmHg, and anamnestically we got information that they never had increased artery pressure.

Forty nine women were excluded from the study, which in the period of the research, avoided to be controlled in the specific time for exam, women which did not do necessary laboratory analyzes (21 women), or have artificial or spontaneous abortion (26 women), and 2 women in which was discovered fatal anomaly. Also, from the study were excluded 67 normotensive and 2 preeclamptic women, because in the certain moment we achieved the necessary total numbers of normotensive and preeclamptic pregnant. These 69 pregnant by the end of pregnancy had between 8 and 13 week of gestation (wg). We reviewed age, education, nationality, parity, smoking status, week of PE onset, duration of PE, duration of pregnancy, birth weight and length, and birth weight in percentile. Smoking status and level of education was determined by self-report.

All subjects were followed until delivery. The gestational age at delivery, obstetric complications if any, and neonatal outcome were recorded. For those subjects who subsequently delivered in another hospital, the obstetric information was obtained by telephoning the subject or via contact with staff in other hospital. Birth weight (to the nearest gram) was classified into five categories: very low birth weight (<5<sup>th</sup> percentile), low (5 -9.9), normal (10-89.9), high (90-94.9) and very high (>95). The US scanning was performed using the US unit *GE LogiqCX 200*, with a convex transabdominal transducer of 3.5 MHz.

HC was obtained using an ellipse in a horizontal section at the level of the thalamus and the cavum septi pellucidi. In the same level was measured and BPD by placing callipers from the outer-to-inner aspects of feta skull. AC was also obtained using an ellipse, in a transverse section of the fetal abdomen at the level where the umbilical vein enters the liver. The FL was measured in longitudinal section by placing callipers at the end of the diaphysis in an image showing both epiphyses. Three measurements were made of each parameter and the mean used in the statistics [9].

Another important use of US is estimating the amount of amniotic fluid. The amniotic fluid index (AFI) was obtained by summing the largest cord-free vertical pocket in each of the four quadrants of an equally divided uterus. The AFI varies with gestational age, but as rule of thumb, the normal AFI falls between 10 and 24 cm after 30 weeks' gestational age [10]. At the same time with fetal biometry and measurement of AFI, we were examined placental maturity. We use Grannum classification (Figure 1), which proposed four distinct grades of placental maturity [11]:



Figure 1: Grannum classification.

- 1) Grade 0: Placental body is homogeneous. The amniochorionic plate is evenin the form of a smoothline(Late 1<sup>st</sup> trimester and early 2<sup>nd</sup> trimester)
- Grade I : Placental body shows a few echogenic densities ranging from 2-4 mm in diameter. Chorionic plate shows small indentations (Mild 2<sup>nd</sup> trimester and early 3<sup>rd</sup> trimester; 18-29 weeks)
- 3) Grade II: Chorionic plate shows marked indentations, creating comma-like densities which extend into the placental substance but do not reach the basal plate. The echogenic densities within the placental also increase in size and number. The basal layer comes punctuated with linear echoes which are enlarged with their long axis parallel to the basal layer (Late 3<sup>rd</sup> trimester; ≥30 weeks to delivery)
- 4) Grade III : Complete indentations of chorionic plate through to the basilar plate creating cotyledons (portions of placenta separated by the indentations; 39 weeks and post dates) [11].

Placental texture Grade III before 34 wg, and grade II before 31 wg, was categorized as preterm placental maturity [11]. Pre-

pregnancy BMI was based on measured height and maternal weight at the initial visit (6-12 wg) and maternal self-report of pre-pregnancy weight. Height was measured by using a portable stadiometer, accurate to 1 mm. Weight was determined by using the average of two measurements, with the woman lightly clothed. A scale accurate 0.2 kg was used. Pre-pregnancy BMI was categorized as: underweight (<19.9), normal (20.0-24.9), overweight (25.0-29.9) or obese (>30.0) [3]. Total maternal weight gain during pregnancy was recorded on admission to delivery ward.

Blood pressure measurements were performed using a mercury sphygmomanometer according to a standardized published protocol, and all urine specimens were assessed for protein by dipstick. Mild Preeclampsia was defined by the occurrence of two or more systolic pressure  $\geq$ 140 mmHg and/ or diastolic pressure  $\geq$ 90 mmHg, diastolic blood pressure measurements, with the first elevated blood pressure occurring after 20 weeks' gestation up to 24 hours after delivery, combined with proteinuria at least 0.3g or "1+ protein" per 24 hours [12].

Severe preeclampsia was defined as a systolic blood pressure of 160 mmHg or greater and diastolic blood pressure of 110 mmHg or greater on at least two occasions at least 4 hours apart or on one occasion if antihypertensive therapy was administered. Severe proteinuria was defined with a 24-hour urine sample containing  $\geq$  3.5 g of protein or two urine samples of "3+ protein" or greater taken at least 4 hours apart. The syndrome of haemolysis elevated liver enzymes, and low platelets and eclampsia was also categorized as severe PE [12].

Quantitative data are presented as the mean values  $\pm$  standard deviation and relative numbers of each group. Also, during the research these methods used were: Student's t test, chi-squared test, Spearman correlation coefficient, ANOVA multivariate and univariate analysis and post-hoc test was used to make the statistical differences and comparisons among the normal, mild preeclamptic and severe preeclamptic pregnant patients. For all comparisons, two-tailed tests were accepted as significant when p<0.05. The data are presented in tables and figures.

## **Results and Discussion**

Maternal characteristics and pregnancy outcomes for the three study groups are shown in Table 1. Using the US method, the abovementioned parameters were monitored with every patient; also examination of the placenta and determination of the amount of amniotic fluid index. Parametric and nonparametric one factorial analysis of variance was used to analyze values of US measurements. Statistical analysis of the biometric parameters received with US in the 20 week of gestation (wg), showed that there isn't obvious difference between groups (p>0.05) regarding the growth and development of the fetus.

Table 1: Description of maternal characteristics and pregnancy outcome by study groups [13].

Characteristics	Controls N=300	Mild Preeclampsia N=67	Severe Preeclampsia N=33	P Value
Maternal Age (years) <20 20-25 26-30 31-35 >35	27.5±5.04 (17-42) 5.3 (16/300) 29.0 (87/300) 40.0 (120/300) 21.0 (63/300) 4.7 (14/300)	27.4±5.9 (17-42) 8.96 (6/67) 40.3 (27/67) 19.4 (13/67) 19.4 (13/67) 11.9 (8/67)	29.2±5.8 (16-43) 9.1 (3/33) 12.1 (4/33) 42.4 (14/33) 24.2 (8/33) 12.1 (4/33)	p>0.05†
Parity (%) Primipara Multipara	46.7 (140/300) 53.3 (160/300)	65.7 (44/67) 34.3 (23/67)	60.6 (20/33) 39.4 (13/33)	p<0.05†
Smoking Status	10.33 (31/300)	1.49 (1/67)	30.3 (1/33)	<0.05‡
BMI <19.99 20.0-24.99 25.0-29.99 Weight Gain (kg)	22.7±1.7 (19.1-27.6) 1.7 (5/300) 87.3 (262/300) 11.0 (33/300) 13.9±3.1 (7-29)	25.53±1.6 (21.8-27.9) 0 (0/67) 23.9 (16/67) 76.1 (51/67) 19.6±3.8 (13-31)	25.8±2.2 (21.7-29.1) 0 (0/33) 30.3 (10/33) 69.7 (23/33) 20.2±7.4 (10-39)	<0.01§
Duration of Pregnancy ≤32 33-36 >37	39.6±0.9 (37-42) 0 (0/300) 0 (0/300) 100 (300/300)	39.1±0.9 (37-40) 0 (0/67) 0 (0/67) 100 (67/67)	37.5±2.0 (32-40) 3.03 (1/33) 18.2 (6/33) 78.8 (26/33)	<0.01†
Birth Weight (g)	3427.8±332.4	2989.3±256.2	2582.4±407.9	<0.01†
Birth Length (cm)	50.7±1.2	48.7±1.3	46.4±2.4	< 0.05 †
Birth Weight (percentile) <10 Oct-90 >90	3 (9/300) 93.3 (280/300) 3.7 (11/300)	29.9 (20/67) 70.2 (47/67) 0 (0/67)	63.6 (21/33) 36.4 (12/33) 0 (0/33)	<0.01†

Data are given as mean, standard deviation and range or % unless otherwise specified;

N: number of subjects; † multivariate analysis; ‡ chi-squared test

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#### Fetal Growth and Body Proportion during Pre-Eclamptic Pregnancy

In the 26 wg there are evident empiric differences in the growth and development of the fetuses from normotensive and hypertensive pregnancies, although, that is still in a period which hypertension is not manifested. US measurement we found similar differences between groups as in 32 wg The US results measured in 26 and 32 wg are showed in Table 2.

**Table 2:** The results from the ultrasound measurements in 26 and 32 weeks of gestations.

Parameter	Groups	n	x	sd	Min-Max	P value	
26 week of gestation							
BPD*	C† MP‡ SP∫	300 67 33	6.66 6.52 6.51	0.242 0.21 0.22	6.05-7.13 6.05-6.82 6.05-6.9	p>0.05	
HC**	C MP SP	300 67 33	24.48 24.12 23.92	0.845 0.79 0.825	22.11-25.9 22.4-25.5 22.4-25.5	p>0.05	
FL§	C MP SP	300 67 33	6.66 6.52 6.51	0.242 0.21 0.22	6.05-7.13 6.05-6.82 6.05-6.9	p>0.05	
AC#	C MP SP	300 67 33	21.95 21.17 21.14	1.03 1.113 1.046	19-24 19-23.4 18.9-23.1	p>0.05	
HC/AC*	C MP SP	300 67 33	1.11 1.14 1.13	0.028 0.031 0.024	0.98-1.23 1.069-1.203 1.099-1.189	p>0.05	
		32 we	ek of ge	station	1		
BPD	C MP SP	300 67 33	8.27 8.07 8.08	0.27 0.21 0.19	7.7-8.91 7.73-8.88 7.74-8.61	p>0.05	
НС	C MP SP	300 67 33	29.88 29.35 29.4	0.92 0.71 0.58	28.15-32.2 27.4-32 28.3-30.97	p>0.05	
FL	C MP SP	300 67 33	6.66 6.52 6.51	0.242 0.21 0.22	6.05-7.13 6.05-6.82 6.05-6.9	p>0.05	
AC	C MP SP	300 67 33	21.95 21.17 21.14	1.03 1.113 1.046	19-24 19-23.4 18.9-23.1	p>0.05	
HC/AC	C MP SP	300 67 33	1.11 1.14 1.13	0.028 0.031 0.024	0.98-1.23 1.069-1.203 1.099-1.189	p>0.05	

\*BPD: Biperietal Diameter; \*\*HC: Head Circumference; §FL: Femur Length; #AC: Abdominal Circumference; \*HC/AC: Head Circumference/Abdominal Circumference Ratio; †C: Control Group; ‡MP: Mild Preeclampsia Group; JSP- Group with Severe Preeclampsia

The results from the US methods between 36 and 40 wg are showed in the Table 3. In 36 wg US measurement we found similar differences between groups as in 32 wg The most obvious differences were regarding the following parameters: BPD, HC, FL and AC. Evident differences between fetuses from hypertensive and normal pregnancies existed when calculating the middle value of the HC/AC. Analyzed US results in 38 wg also showed high obvious empiric difference regarding all parameters. Statistical differences was on the level p<0.05.

**Table 3:** The results from the ultrasound measurements between 36-40weeks of gestations.

Parameter	Groups	n	X	sd	Min-Max	P value		
	36 week of gestation							
*BPD	†C ‡MP ∫SP	300 67 29	9.08 8.92 8.85	0.22 0.21 0.22	8.58-9.47 8.5-9.41 8.5-9.27	p>0.05		
**HC	C MP SP	300 67 29	32.92 32.4 32.08	0.79 0.74 0.73	31.1-34.5 30.5-34.5 30-5-33.41	p>0.05		
§FL	C MP SP	300 67 29	7.09 6.8 6.71	0.27 0.31 0.3	6.4-7.7 6.3-7.7 6.4-7.3	p>0.05		
#AC	C MP SP	300 67 29	32.39 31.35 30.78	1.57 1.41 1.22	21.8-34.9 28.2-34.9 29.3-33.3	p>0.05		
*HC/AC	C MP SP	300 67 29	1.015 1.037 1.044	0.024 0.027 0.021	0.96-1.107 0.988-1.1 1.003-1.075	p>0.05		
	38 week of gestation							
BPD	C MP SP	296 63 20	9.38 9.23 9.13	0.15 0.16 0.2	8.97-9.67 8.8-9.51 8.8-9.47	p>0.05		
НС	C MP SP	296 63 20	34.26 33.51 33.1	0.04 0.85 0.87	32-36.5 32-35.79 32-35.77	p>0.05		
FL	C MP SP	296 63 20	7.51 7.15 7.01	0.31 0.33 0.39	6.9-8 6.5-7.97 6.5-7.91	p<0.05		
AC	C MP SP	296 63 20	34.35 32.82 32.19	1.37 1.43 1.32	29.7-26.6 30.4-35.9 30.4-35.1	p<0.05		
HC/AC	C MP SP	296 63 20	0.997 1.021 1.028	0.022 0.027 0.022	0.96-1.119 0.98-1.07 0.985-1.057	p<0.05		
		40 we	ek of ge	station				
BPD	C MP SP	183 26 6	9.52 9.32 9.31	0.14 0.15 0.16	9.17-9.85 9-9.58 9.13-9.49	p>0.05		
НС	C MP SP	183 26 6	34.95 33.86 33.93	0.81 0.69 0.93	33-36.8 32.5-35.6 33-35.2	p>0.05		
FL	C MP SP	183 26 6	7.77 7.29 7.2	0.22 0.33 0.54	7-8.2 6.8-7.9 6.43-7.8	p>0.05		
AC	C MP SP	183 26 6	35.37 33.5 33.42	0.98 1.37 1.94	32.9-37.5 31-35.8 31-35.5	p>0.05		
HC/AC	C MP SP	183 26 6	0.987 1.012 1.017	0.012 0.026 0.035	0.953-1.018 0.97-1.056 0.97-1.065	p>0.05		

\*BPD: biperietal diameter; \*\*HC: Head Circumference; §FL: Femur Length; #AC: Abdominal Circumference; \*HC/AC: Head Circumference/Abdominal Circumference Ratio; †C: control group; ‡MP: Mild Preeclampsia Group; ∫SP: Group With Severe Preeclampsia

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#### Fetal Growth and Body Proportion during Pre-Eclamptic Pregnancy

Last US exam was performed in the 40 wg, in pregnancies which came to their controlled as scheduled, which pregnancy age was at least 39 + 1 wg. Also in 40 wg were measured the same parameters like in the previous US exams. With this exam too, is concluded obvious difference between the groups regarding the fetus growth. The most differences in the middle values are at the AC and FL, although the other parameters were difference, too. With statistical analyzes is not found statistical obvious difference (p>0.05).

However, the empirical values shown in Table 3, we can notice that there are significant differences in average values. Thus, BPD and HC, which parameters were affected at least in the last control we observed difference of 3 weeks of gestation compared with referents values and values obtained in fetuses from normotensive pregnancy. Similar differences exist with other parameters, and increased HC/AC ratio, indicates to asymmetric IUGR.

The results and the differences in the growth of BPD, HC, FL, AC and HC/AC ratio are presented in the Figures 2-6. During the pregnancy, with US are evaluated placenta and was measured AFI. Examined results in the 20 wg showed that there was no difference between the groups, considering the fact that in all pregnancies (group A and group B) the degree of placental maturity was 0, and the amount of amniotic fluid in all cases was.



Figure 2: BPD growth.



Figure 3: HC growth.





Figure 5: AC growth.



Figure 6: HC/AC ratio during pregnancy.

The results of US scanning of the placenta in the period between 26 and 40 wg are presented in Table 4. Using chi-quadrate test we found statistically significant difference between the groups (p<0.05), which difference continued to the end of pregnancy. The results suggested that it is difficult to form of PE is greater preterm maturing and aging of the placenta. Another important use of US is estimating of the AFI. A decreased volume of amniotic fluid is closely associated with PE and IUGR.

Table 4: Degrees of placental maturation between 26 and 40 wg.

Grade in 26	Controls	Mild PE	Severe PE
w.g	(n=300)	(n=67)	(n=33)
0	86.33	41.79	51.52
I	13.67	58.21	48.48
Grade in 32	Controls	Mild PE	Severe PE
w.g	(n=300)	(n=67)	(n=33)
I	81.33	55.22	45
II	18.67	44.78	52
III	0	0	3
Grade in 36	Controls	Mild PE	Severe PE
w.g	(n=300)	(n=67)	(n=29)
I	0.67	0	0
II	82.33	61.19	65.52
III	17	38.81	34.48
Grade in 38	Controls	Mild PE	Severe PE
w.g	(n=296)	(n=63)	(n=20)
II	26.01	6.35	5
III	73.99	93.65	95
Grade in 40	Controls	Mild PE	Severe PE
w.g	(n=183)	(n=20)	(n=6)
II	1.09	5	0
III	98.91	95	100

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Based on the values of AFI, we determined whether the amount of amniotic fluid decreased or increased. From 26 to 40 wg in terms of amniotic fluid volume, the difference was statistically significant at the level p <0.05. Obtained results are shown Table 5. PE complicated pregnancies have potentially negative influence on the fetal growth and it is increasing the perinatal morbidity and mortality. In the present study, severe PE was associated with lighter, shorter and leaner newborns, more than newborns from mild PE pregnancy.

AFI (26 w.g)	Controls	Mild PE	Severe PE
	(n=300)	(n=67)	(n=33)
Normal	100	94.03	90.91
Reduced	0	5.97	9.09
increased	0	0	0
AFI (32 w.g)	Controls	Mild PE	Severe PE
	(n=300)	(n=67)	(n=33)
Normal	97	85.07	60.61
Reduced	1.33	11.94	36.36
increased	1.67	2.99	3.03
AFI (36 w.g)	Controls	Mild PE	Severe PE
	(n=300)	(n=67)	(n=29)
Normal	83.34	50.75	44.83
Reduced	15.33	46.27	55.17
increased	1.33	2.99	0
AFI (38 w.g)	Controls	Mild PE	Severe PE
	(n=296)	(n=63)	(n=20)
Normal	49.32	11.11	15
Reduced	50.34	87.30	85
increased	0.34	1.59	0
AFI (40 w.g)	Controls	Mild PE	Severe PE
	(n=183)	(n=26)	(n=6)
Normal	7.65	7.69	0
Reduced	92.35	92.31	100
Increased	0	0	0

The newborns from the hypertensive pregnancies had lower birth weight (approximate birth weight for MP group was 2989.25 $\pm$ 256.19g and for Severe PE was 2582.42 $\pm$ 407.85g.) vs. neonates from normotensive pregnancies (3427.77 $\pm$ 332.36g). Body length was also different between the groups. The newborn's birth measurements from the Mild PE were 48.67 $\pm$ 1.33 cm and for the group SP 46.42 $\pm$ 2.36 vs. neonates from normotensive pregnancies (50.65 $\pm$ 1.2cm; p<0.05). Also, these results, too, are same as from the associated literature in this area [5,7,14,15].

Our study includes data of smoking status. It is well know that smoking is a strong and common risk factor for low birth weight. Smoking seems to be negatively associated with PE. Thus, adjusting for smoking would increase rather than decrease the effect of PE in infants' size [16]. The US made every obstetrician's dream comes true, opening a window in the intra-uterine content, allowing fetus growth and development observation, as well as examining the placenta and determining the amount of amniotic fluid; and all of that is safe, direct, intentional and repeatable. Fetal growth measured with US with other risk factors could predict development of PE and poor neonatal outcomes [7,8]. IUGR in the ultrasound presents reducing the growth speed of the fetal parameters, which is lower than the physiological recession [4,5,17]. With the gestation advance, the individual growth variability is also increased regarding the standards. It is considered that all fetuses until 20 wg have the same growth formula. The importance of knowing the technological parameters for US device, which is used in the practice, is emphasized in order to get adequate information regarding the state and fetus development.

The fetal body parts most frequently used to evaluate growth includes BPD, HC, AC and FL. By measuring the BPD and HC we can indirectly follow the growth of the fetal brain. Cephalometry didn't showed obvious differences between the groups. BPD and HC measurement in this report suggest that not exist statistical differences between fetuses from normotensive and hypertensive pregnancies (p>0,05), but biggest deviations these parameters exist in the fetus in pregnancy with severe form of PE.

AC is useful in assessing nutritional status in normal and altered states of fetal growth, because it encompasses the liver and subcutaneous tissue in that area, both of which show reduction size secondary to chronic hypoxia and decrease in substrate, associated with IUGR [9,18].

Regarding AC we found biggest differences, especially after 26 wg. Measuring FL can help to edit the US growth profile, even though same as BPD, this parameter, too, could show undetected IUGR. The Japanese authors found that lower values of FL and HL in the first 20 wg, are showing increased risk of structural malformation (especially cardiovascular and genetical anomalies) more than declined growth or slower fetus growth [19].

Calculate the HC/AC ratio, in our research has shown that there is increased HC/AC ratio in the fetuses of hypertensive pregnancy, especially those with severe form of PE. Empirical difference is evident after 26 wg, although statistical no significant difference (p> 0.05). This increased HC/AC ratio speaks in favor of asymmetric IUGR.

Our results are similar as the one from the available literature; in PE, most often is developed asymmetrical type of IUGR which mostly is developed in the third quarter of the pregnancy. In conditions of UPC it comes to redistribution of the circulation, where the brain tissue and the top body parts get enough amount of blood. In these conditions the most affected is the bottom part of the body (AC and FL) [20,21].

During the research we followed the maturation of placenta. The results are shown Table 5. From these results we can be concluded that the PE, present premature aging placenta, which is more pronounced for severe forms of PE. The difference was statistically significant (p < 0.05). Using the US method, we concluded that the PE is disorder that is associated IUGR, preterm aging of placenta and reduced AFI, i.e. olighoamnion. Statistically significant difference was noted even at 26 wg, which is held by the end of pregnancy on the level of p < 0.05.

# Conclusion

Results of our study suggested that inadequate fetal growth measured with US is associated with an increased risk of PE. With US scan the changes in the fetus development can be detected, also fast placenta aging, even before increased artery blood pressure above normal values, which makes US diagnostically the best option antenatal detection of restricted fetal development and growth [22].

Our results support the hypothesis that PE is a heterogeneous disorder and that it may appear in at least two forms [17]: restricted fetal growth PE and normal fetal growth PE. Patients with restricted fetal growth PE often deliver prior to term. Preeclamptic pregnant with normal fetal growth often deliver at term.

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## References

- 1. James PR, Nelson-Piercy C (2004) Management of hypertension before, during, and after pregnancy. Heart 90(12):1499-1504.
- Assis RT, Viana PF, Rassi S (2008) Study on the Major Maternal Risk Factors in Hypertensive Syndromes. Arq Bras Cardiol 91(1): 11-16.
- Yinon Y, Nevo O, Many A, Rolfo A, Todros T, et al. (2008) Severe Intrauterine Growth Restriction Pregnancies Have Increased Placental Endoglin Levels. Am J Pathol 172(1): 77-85.
- Andrea Lausman A, McCarthy FP, Walker M, Kingdom J (2012) Screening, Diagnosis, and Management ofIntrauterine Growth Restriction. J Obstet Gynaecol Can 34(1): 17-28.
- Mandruzzato G, Antsaklis A, Botet F, Chervenak F, Figueras F, et al. (2008) Intrauterine restriction (IUGR), recommendations and guidelines for perinatal practice. J Perinatt Med 36(4): 277-281.
- Vilar J, Merialdi M, Gulmezoglu M, Abalos E, Carroli G, et al. (2003) Nutritional interventions during Pregnancy for the Prevention or Treatment of Maternal morbidity and Preterm Delivery: Overview of Randomized Controlled trials. J Nutr 133(5 Suppl 2): 1606S-1625S.
- Ramussen S, Irgens ML (2008) History of fetal growth restriction is more strongly associated with severe rather than milder pregnancyinduced hypertension. Hypertension 51(4): 1231-1238.
- 8. Alberry M, Soothil P (2007) Management of fetal growth restriction (guidelines). Arch Dis Child Fetal Neonatal Ed 92(1): F62-F67.

- 9. Abuhamad A, Chaoui R, Jeanty P, Paladini D, Walsh E (2014) Ultrasound in Obstetrics and Gynecology: A Practical Approach.
- Ahmed B, Adra A, Kavak ZN (2009) Ultrasound in Obstetrics and Gynecology. Ahmed B. Ed. Donal School. Jaypee Brithers Medical Publisher.
- Walker MG, Hindmarsh PC, Geary M, Kingdom JCP (2010) Sonographic Maturation of the Placenta at30 to 34 Weeks Is Not Associated With Second Trimester Markers of Placental Insufficiency in Low-risk Pregnancies. J Obstet Gynaecol Can 32(12): 1134-1139.
- Glanville T, Walker JJ (2007) Management of mild pre-eclampsia. In: Lyall F & Belfort M (Eds.), Pre-eclampsia, Etiology and Clinical Practice. Cambridge University Press, Cambridge, UK, pp. 357-368.
- Jašović-Siveska E, Jašović V (2011) Prediction of mild and severe preeclampsia with blood pressuremeasurements in first and second trimester of pregnancy. Ginekol Pol 82(11): 845-850.
- 14. Rasmussen S, Irgens ML (2003) Fetal growth and body proportion in preeclampsia. Obstet Gynecol 101(3): 575-583.
- Coutts J (2007) Pregnancy-induced hypertension-the effects on the newborn. In: Lyall F & Belfort M (Eds.), Pre-eclampsia, Etiology and Clinical Practice. Cambridge University Press, Cambridge, UK, pp. 506-521.
- Ness BR, Zhang J, Bass D, Klebanoff AM (2008) Interreaction between smoking and weight in pregnancies complicated by preeclampsia and small-for-gestational age. Am J Epidemiol 168(4): 427-433.
- 17. Morris KR, Khan SK, Coomarasamy A, Robson CS, Kleijnen J (2007) The value of predicting restriction of fetal growth and compromise of its well being: Systematic quantitative overviews (meta-analysis) of test accuracy literature. BMC Pregnancy and Childbirth 7: 3.
- Xiong X, Demianczuk NN, Dunkan- Saunders L, Wang FL, Fraser DW (2002) Impact of Preeclampsia and Gestational Hypertension on Birth Weight by Gestational Age. Am J Epidemiol 155(3): 203-209.
- 19. Bamfo JEAK, Odibo AO (2011) Diagnosis and Management of Fetal Growth Restriction. Journal of Pregnancy.
- Mutter WP, Karumanchi SA (2008) Molecular mechanisms of preeclampsia. Microvasc res 75(1): 1-8.
- 21. Hobbins J (1997) Morphometry of fetal growth. Acta Pediatr 423: 165-168.
- 22. Jasovic-Siveska EI, Jasovic VI (2008) Real-time ultrasound in the detection of intrauterine growth retardation in preeclampsia. Bratisl Lek Listy 109(9): 405-411.